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EXAMINER	
SPIEGLER, ALEXANDER H	
ART UNIT	PAPER NUMBER
1637	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/016,349	RECIPON ET AL.	
	Examiner	Art Unit	
	Alexander H. Spiegler	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) *6,10-14,16 and 17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7-9 and 15* is/are rejected.

7)☒ Claim(s) *1-5,7-9 and 15* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4/15/03* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Application

1. Currently, claims 1-17 are pending. Claims 1-5, 7-9 and 15 have been rejected herein and Claims 6, 10-14 and 16-17 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.151(b) and MPEP § 821. This action is made NON-FINAL.

Election/Restrictions

2. Applicant's election with traverse of Group I (Claims 1-5, 7-9 and 15, and SEQ ID NO: 51 (encoding SEQ ID NO: 174)) in Applicant's response of October 21, 2003 is acknowledged.

Applicants argue the search of all the claims would be overlapping and would not cause a serious burden on the Examiner. This argument has been considered, but is not persuasive, since a serious burden on the examiner may be prima facie shown if the examiner shows by appropriate explanation either separate classification, separate status in the art, or a different field of search as defined in MPEP § 808.02. In the instant case, the serious burden of search has been established by, at least, the different classification of the inventions (see restriction requirement and Applicant's remarks on pages 1 and 2, separately classifying each group).

Applicants also argue that ten sequences should be examined. This argument has been considered, but is not persuasive, for several reasons. First, MPEP 803.04 states that "*up to* ten independent and distinct nucleotide sequences will be examined", which therefore, does not require that 10 sequences must always be searched. Additionally, due to the large number of sequences that have been added to sequence databases (especially since November 19, 19174 and following the sequencing of the human genome), it is a serious burden for the Office to examine more than one sequence.

Accordingly, for these reasons, and those of record, the restriction requirement is maintained.

3. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R. § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 C.F.R. § 1.48(b) and by the fee required under 37 C.F.R. § 1.17(h).

CRF/Sequence Notes

4. The Sequence Listing filed in this application complies with the requirements of 37 CFR 1.821-1.825 and has been entered.

Claim Objection

5. Claims 1-5, 7-9 and 15 are objected to because the claims recite non-elected subject matter. Applicants should amend the Claims to recite the elected sequence, SEQ ID NO: 51 (encoding SEQ ID NO: 174). The claims have been interpreted as being drawn to only the elected sequences.

Appropriate correction is required.

Information Disclosure Statement

6. The information disclosure statement filed on April 15, 2003 complies with CFR 1.97, 1.98, and M.P.E.P. 609, and has been considered (see enclosed signed PTO-1449).

Specification

7. The disclosure is objected to because of the following informalities:

A) On page 75, line 15, an underscore sign appears, wherein, the specification recites, "yeast_mating factor". Applicants can overcome this objection by deleting the underscore, "_".

B) The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. (See page 54, lines 21-31 and page 135, line 24, for example). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

C) The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-5, 7-9 and 15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1-5, 7-9 and 15 over "selectively hybridizes" because it is not clear as to what is meant by "selectively hybridizes". That is, it is not clear as to what conditions are required for "selective hybridization". The specification does not specifically define what conditions are necessary for "selective hybridization", nor does the prior art teach such specific conditions. Accordingly, it is suggested that Applicants amend the claims to recite specific hybridization conditions (e.g., xSSC, temperature, etc.).

B) Claims 1-5, 7-9 and 15 are indefinite over Claim 1(d), because it is not clear as to how "a nucleic acid molecule having at least *60% sequence identity* to the nucleic acid molecule of (a) or (b)" can encode an amino acid sequence of SEQ ID NO: 174 (the protein encoded by SEQ ID NO: 51). (emphasis added). First, it is not clear as to how a nucleic acid molecule that has a 60% sequence identity to SEQ ID NO: 51 or a nucleic acid that molecule that encodes SEQ ID NO: 174, can also encode SEQ ID NO: 174. That is, if the nucleic acid molecule of (d) has *only* a 60% sequence identity to a sequence that encodes SEQ ID NO: 174, it is not clear the nucleic acid of (d) *can* also encode SEQ ID NO: 174. The specification does not provide any teachings as to what nucleic acids can be mutated and still encode SEQ ID NO: 174. Accordingly, it is not clear as to how "a nucleic acid molecule having at least *60% sequence identity* to the nucleic acid molecule of (a) or (b)" can encode an amino acid sequence of SEQ ID NO: 174.

Claim Rejections - 35 USC § 101

10. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

11. Claims 1-5, 7-9 and 15 rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a substantial asserted utility, or a well-established utility.

The pending claims have been reviewed in light of the Utility Examination Guidelines in the Federal Register, Vol. 66, No. 4, pages 1092-1099, Friday, January 5, 2001, as well as the MPEP and existing law.

I. *The specification does not assert a substantial utility because the utilities asserted by Applicants requires or constitutes carrying out further research to identify or reasonably confirm a "real world" use.*

Applicants assert the claimed nucleic acid can be used in methods "for identifying, diagnosing, monitoring, staging, imaging and treating lung cancer and non-cancerous disease states in lung." (see page 7, lines 22-24).

The specification teaches a data mining experiment for identifying nucleic acids (see pages 116-120). Specifically, the specification teaches SEQ ID NO: 51 was identified by data mining of sequences in the Incyte Genomics LIFESEQ database using CLASP software (see pages 116-118). That is, SEQ ID NO: 51 was procured from, and thereby known by Incyte Genomics Inc. (see page 116). Applicants allege that SEQ ID NO: 51 is considered to have a "CLASP 2CLASP1" profile (page 118, line 45), wherein:

> To qualify as a CLASP 2 candidate, a gene must exhibit detectable expression in tumor tissues and undetectable expression in libraries from normal individuals and libraries from normal tissue obtained from diseased patients. In addition, such a gene must also exhibit further specificity for the tumor tissues of interest.
>
> To qualify as a CLASP 1 candidate, a gene must exhibit statistically significant expression in the tissue of interest compared to all other tissues. Only if the gene exhibits such differential expression with a 90% of confidence level is it selected as a CLASP 1 candidate.

(see page 117, lines 12-16 and lines 22-26).

The specification is silent with respect to any potential nucleic acids that fall within Claim 1(c) or (d) (i.e., there is not CLASP profile for these nucleic acids).

Other than Applicants characterization that SEQ ID NO: 51 has a "CLASP2CLASP1" profile, there is no data or experimental analysis of SEQ ID NO: 51 or the other claimed nucleic

acids. That is, the specification does not teach what tissues were used, whether diseased and normal samples were expressed and then compared against one another, how many patients these results stem from, relative expression levels of tissues, and furthermore, it is not clear as to what was the source of the nucleic acids (e.g., cell lines or primary tumor cells).

MPEP § 2107.01 states:

> A "substantial utility" defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities... An assay that measures the presence of a material which has a stated correlation to a predisposition to the onset of a particular disease condition would also define a "real world" context of use in identifying potential candidates for preventive measures or further monitoring.

In the instant case, further research to identify or reasonably confirm a "real world" context of use would be required. For example, in order for a nucleic acid to be useful for detection, diagnosis and/or treatment of a disease, there must be a well established or disclosed correlation or relationship between the claimed nucleic acid and a disease or disorder. The presence of a nucleic acid in tissue that is derived from cancer cells is not sufficient for establishing a utility in diagnosis of disease in the absence of some information regarding a correlative or causal relationship between the expression of the claimed nucleic acid and the disease. If a molecule is to be used as a surrogate for a disease state, some disease state must be identified in some way with the molecule. There must be some expression pattern that would allow the claimed nucleic acid to be used in a diagnostic manner. Many nucleic acids are expressed in normal tissues and diseased tissues. Therefore, one needs to know, e.g., that the claimed nucleic acid is either present only in cancer tissue to the exclusion of normal tissue or is expressed in higher levels in diseased tissue compared to normal tissue (i.e. overexpression). Evidence of a differential expression might serve as a basis for use of the claimed nucleic acid as a diagnostic for a disease. However, in the absence of any disclosed relationship between the

claimed polynucleotide or the protein that is encoded thereby and any disease or disorder and the lack of any correlation between the claimed polynucleotide or the encoded protein with any known disease or disorder, any information obtained from an expression profile would only serve as the basis for further research on the observation itself. "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing." *Brenner* v. *Manson*, 148 USPQ 6174 (US SupCt 11746).

Specifically, in the instant case, the specification does not provide any assay or evidence that clearly demonstrates a correlation between SEQ ID NO: 51 (or nucleic acids encompassed by Claim 1, (c) or (d)) and methods for identifying, diagnosing, monitoring, staging, imaging and treating lung cancer and non-cancerous disease states in lung. That is, the specification does not teach any assay or expression analysis that indicates the relationship between SEQ ID NO: 51 (or nucleic acids encompassed by Claim 1, (c) or (d)) and lung cancer. At best, Applicants have proposed a starting point for further research in order to determine whether SEQ ID NO: 51 is correlated with lung cancer. Accordingly, the disclosure does not present a substantial utility that would support the requirement of 35 U.S.C. 101.

II. *The specification is not supported by a well-established utility because one of ordinary skill in the art would not immediately appreciate why the invention is useful based on the characteristics on the invention.*

MPEP 2107 states:

> An invention has a well-established utility if (i) a person of ordinary skill in the art would immediately appreciate why the invention is useful based on the characteristics of the invention (e.g., properties or applications of a product or process), and (ii) the utility is specific, substantial, and credible."

Applicants have provided little to no evidence of the characteristics of the claimed nucleic acids, the asserted utility is not substantial, and based on Applicants assertion that the

claimed nucleic acid is new (see page 1, lines 9-10), it is not apparent as to how "a person of ordinary skill in the art would immediately appreciate why the invention is useful". This is evidenced by the fact that further research would need to be carried out by the skilled artisan even given Applicants' claimed nucleic acids (see above). For these reasons, the specification is not supported by a well-established utility.

Accordingly, the claimed invention lacks a substantial and well-established utility.

Claim Rejections - 35 USC § 112

12. Claims 1-5, 7-9 and 15 also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Furthermore, in addition to the reasons above, the specification is further not enabling because the specification does not establish that in the general population SEQ ID NO: 51 is overexpressed in lung tumor versus other tumor cells or versus normal cells.

MPEP 2164.01 states:

> Even though the statute does not use the term 'undue experimentation,' it has been interpreted to require that the claimed invention be enabled so that any person skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

The *Wands* court outlined several factors to be considered in determining whether a disclosure would require undue experimentation. These factors include, but are not limited to:

(1) the quantity of experimentation necessary, (2) the amount of direction or

guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims." *Id.* at 1404.

In the instant case, the specification does not enable one of skill in the art to make and use the claimed invention for the following reasons:

(1) ***Nature of the Invention & Breadth of the Claims***

The claims are drawn to isolated nucleic acid molecules comprising a nucleic acid sequence encoding SEQ ID NO: 174, "a" nucleic acid of SEQ ID NO: 51, nucleic acid molecules that "selectively hybridize" to a nucleic acid that encodes SEQ ID NO: 174 or "a" nucleic acid of SEQ ID NO: 51, and nucleic acids having at least 60% sequence identity to a nucleic acid sequence encoding SEQ ID NO: 174 or "a" nucleic acid of SEQ ID NO: 51.

Thus, the claims are drawn to a large genus of possible nucleic acids, including sequences from other species, mutated sequences, and allelic variants having different functional activities than that of the nucleic acids of SEQ ID NO: 51, and nucleic acids encoding the polypeptide of SEQ ID NO: 174.

(2) ***Relative Skill of those in the Art, State of the Prior Art, Amount of Direction or Guidance Presented & Presence or Absence of Working Examples***

The specification teaches SEQ ID NO: 51 was procured from, and thereby known by Incyte Genomics Inc. (see page 116). However, the specification does not provide any working examples of using the claimed nucleic acids for identifying, diagnosing, monitoring, staging, imaging and treating lung cancer and non-cancerous disease states in lung. Additionally, the specification does not provide any evidence the claimed nucleic acids can be in fact be used in

identifying, diagnosing, monitoring, staging, imaging and treating lung cancer and non-cancerous disease states in lung.

Furthermore, the specification does not teach several elements that would be necessary to enable the skilled artisan to use the nucleic acids of the invention. First, it is not clear as to what the source of the library is (e.g., primary tumor cells versus a cell line) from which the claimed nucleic acids were obtained from. This is an important inquiry, since gene expression in primary tumor cells is often distinct from that which occurs in cell lines (see Dermer et al. Bio/Technology (1994) 12: 320). Assuming Applicants procured the claimed nucleic acids from a primary tumor, the specification does not teach how many samples are present in the library. If Applicants derived expression results from a library containing only one sample, any expression data would not be applicable to the general population. That is, data from one individual is not representative of data that will or may occur in other diseased or normal patients. Thus, even assuming the specification teaches the claimed nucleic acids are overexpressed in lung tumor cells obtained from a single source, the specification has not established that in the general population that the claimed nucleic acids are overexpressed in lung tumor versus normal cells. Additionally, the specification does not teach a comparative readout of expression data among lung tissue (if tested) versus expression of the claimed nucleic acids in other tissues. There is no data showing overexpression in lung tumor cells versus other tumor cell types (e.g., from ovary, breast, etc.) or normal tissue cells (e.g., from lung, ovary, breast, etc.). Furthermore, the specification does not teach what sequences were being compared in the CLASP analysis, what tissues were involved, what types of individuals were screened, and what activity or function the polypeptide of SEQ ID NO: 174 has.

With respect to Claim 1(c) and (d), the claims are drawn to a plurality of possible nucleotide sequence variants of SEQ ID NO: 51, wherein the specification does not provide any guidance as to how to make or alter nucleic acid sequences falling within Claim 1(c) and (d), nor does it teach how to use said sequences. Specifically, the specification is silent as to how nucleotide sequences falling within Claim 1(c) and (d) can be mutated and still have the function of encoding SEQ ID NO: 174, nor does the specification teach any variants of SEQ ID NO: 51. Furthermore, the specification does not teach the critical domains, if any, of the polypeptide encoded by the nucleotide sequences falling within Claim 1(c) and (d).

Accordingly, the relative skill in the art is high, there are no working examples provided for using the claimed nucleic acids, and the specification has provided little to no guidance for using the claimed nucleic acids.

(3) ***Quantity of Experimentation Necessary & the Unpredictability of the Art***

Case law has established that "(t)o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" *In re Wright* 990 F.2d 1557, 1561. In *In re Fisher*, 517 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) it was determined that "(t)he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art". The amount of guidance needed to enable the invention is related to the amount of knowledge in the art as well as the predictability in the art.

In the instant case, the specification, nor the prior art teach an association/and or correlation for SEQ ID NO: 51 (or nucleic acids encompassed by Claim 1(c) or (d)), and therefore, the skilled artisan would not know how to use the claimed nucleic acids. Any

potential results that the skilled artisan would arrive at would be unpredictable given the lack of guidance in the specification and the prior art (see above). For example, the specification teaches that the tumor of interest (i.e., lung tumor library) was compared to normal libraries for all tissues (see page 117). However, it is not clear as to whether all the normal tissues were combined, since there is no expression data for any tissues. It is especially noted that there is no data of normal lung expression. However, assuming that SEQ ID NO: 51 is overexpressed, and the specification only teaches the expression of combined normal tissues (versus normal lung tissue expression), the skilled artisan would not know how to practice the invention because it is not clear as to what level of expression is associated with cancer. Additionally, given the lack of guidance in the specification or the prior art, as to how to alter the claimed nucleotide molecules and retain the activity of SEQ ID NO: 174, the making and using of the nucleic acid molecules encompassed by the claimed invention would also be unpredictable. Finally, the suitability of cell lines, as general models for primary tumors are also unpredictable. For example, Dermer (cited above) teaches:

> [w]hen a normal or malignant body cell survives a crisis period and adapts to immortal life in culture, it takes an evolutionary type step that enables the new cell line to thrive in its artificial environment...Yet normal or malignant cells in vivo are not like that. This means that cell lines are really a new life form on Earth, neither human nor animal. Evidence of the contradictions between life on the bottom of the lab dish and in the body has been in the scientific literature for more than 30 years, evidence that has been systematically ignored by the cancer establishment.

(1st column, page 320).

Therefore, if the nucleic acids in Example 1 were procured from cell lines, then extrapolating expression data from SEQ ID NO: 51 for identifying, diagnosing, monitoring,

staging, imaging and treating lung cancer and non-cancerous disease states in lung would be highly unpredictable.

In order to carry out making and using of the claimed nucleic acids, the experimentation required by the skilled artisan would be considered undue. First, the skilled artisan would have to experiment by altering any of the plurality of possible sequences encompassed by the claims to determine what sequences can be altered, and how they can be altered, and still retain the function of SEQ ID NO: 174. Additionally, once the sequences were obtained, the skilled artisan would have to carry out expression analysis studies on many samples from different tissues from both normal and diseased test subjects (including normal and malignant lung tissues from cell culture and patients' samples, as well as, in cells from unrelated tissues). Following this experimentation, the skilled artisan would have to determine whether the sequences are specific for a disease state. Significance of any increased expression levels needs to be established; as there are usually variations in tissues obtained from different individuals, therefore studies involving statistically significant numbers of patients would also need to be performed. Such experimentation requires a large amount of trial and error analysis, with little to no starting point, absent any teaching in the specification (see above), wherein the results of such analysis are unpredictable, and is therefore considered undue.

In essence, the experimentation that one skilled in the art would be required to perform is in fact the proposed novelty of the invention. However, "(I)t is the specification, not the knowledge of one skilled in the art that must supply the novel aspects of the invention in order to constitute adequate enablement". (*Genetech Inc. v Novo Nordisk* 51 USPQ2d 1001).

Accordingly, in view of the unpredictability in the art and in view of the lack of specific disclosure in the specification, undue experimentation would be required to practice the invention as it is claimed.

Written Description

13. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

14. Claims 1-5, 7-9 and 15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims 1-5, 7-9 and 15 are directed to nucleic acids comprising a nucleic acid sequence encoding SEQ ID NO: 174, "a" nucleic acid of SEQ ID NO: 51, nucleic acid molecules that "selectively hybridize" to a nucleic acid that encodes SEQ ID NO: 174 or "a" nucleic acid of SEQ ID NO: 51, and nucleic acids having at least 60% sequence identity to a nucleic acid sequence encoding SEQ ID NO: 174 or "a" nucleic acid of SEQ ID NO: 51.

Applicants disclose SEQ ID NO: 51.

Claims reciting "comprising", "a" nucleic acid of SEQ ID NO: 51, "at least 60% sequence identity" or nucleic acids that "selectively hybridize" to a nucleic acid that encodes SEQ ID NO: 174 or "a" nucleic acid of SEQ ID NO: 51, are inclusive of sequences from other species, mutated sequences, allelic variants, full-length genes, genomic DNA, for example, all

which have different functions than that of the nucleic acid in SEQ ID NO: 51 or the nucleic acid encoding SEQ ID NO: 174. Thus, the claims broadly encompass many types of nucleic acids (e.g., allelic variants, mutated sequences, genomic DNA, etc.), whereas, the specification only teaches SEQ ID NO: 51.

The specification does not reasonably convey to one skilled in the art that Applicants were in possession of the claimed invention, because the specification does not describe the specific structures (e.g., promoters, enhancers, 5' or 3' untranslated regions), which are found in genomic DNA (i.e., which is encompassed by the instant claims), or any of the other types of nucleic acid molecules encompassed by the broadly claimed invention. More specifically, the specification only describes SEQ ID NO: 51 (which encodes SEQ ID NO: 174), but does not describe the other types of nucleic acid molecules encompassed by the claims.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in *possession* of the invention. The invention is, for purposes of the written description inquiry, *whatever is now claimed* (See page 1117)." (emphasis added)

Additionally, in *The Regents of the University of California v. Eli Lilly* (51 USPQ2d 1398-1412), the court held that a generic statement, which defines a genus of nucleic acids by only their functional activity, does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a

DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

In analyzing whether the written description requirement is met for a genus claim, it is first determined whether a representative number of species have been described by their complete structure. In the instant case, one member of the broadly claimed genus has been defined by structure, i.e., SEQ ID NO: 51. No genomic sequences flanking SEQ ID NO: 51, nucleic acids sequences having at least 60% sequence identity to SEQ ID NO: 51 (which encode SEQ ID NO: 174), nucleic acid molecules that "selectively hybridize" to a nucleic acid that encodes SEQ ID NO: 174 or "a" nucleic acid of SEQ ID NO: 51 have been defined by structure. It is then determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics (e.g., location of intron/exon boundaries, length of introns, length of 5' or 3' untranslated regions, which nucleic acids can be altered to have at least 60% sequence identity to SEQ ID NO: 51 and encode SEQ ID NO: 174, etc.). In the instant case, no such identifying characteristics have been provided for any of the claimed nucleic acids. While at the time of filing, Applicants were in possession of SEQ ID NO: 51, Applicants were not in possession of the broadly claimed genus.

Applicant's attention is also drawn to the "Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, 1st Paragraph, Written Description Requirement" (published in Federal Register/Vol. 66, No. 4/Friday, January 5, 2001/Notices; p. 1099-1111).

Accordingly, because the specification does make clear that Applicants were in possession of the claimed invention at the time the application was filed, and because the claims

are broadly drawn to encompass other nucleic acid molecules not taught or described in the specification, the claims lack adequate written description.

Claim Rejections - 35 USC § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (f) he did not himself invent the subject matter sought to be patented.

16. Claims 1-2 and 4-5 are rejected under 35 U.S.C. 102(a) as being anticipated by LIFESEQ™ Database.

The specification at page 116 states that the nucleic acids of the present invention (including SEQ ID NO: 51) were procured from, and thereby known by Incyte Genomics Inc. (via the Incyte Genomics LIFESEQ database) at the time the invention was made. Accordingly, the nucleic acids of the present invention were known and used in the art prior to the filing of the instant application. The nucleic acid appears to be cDNA from human samples (claims 2 and 4-5).

17. Claims 1-2 and 4-5 are rejected under 35 U.S.C. 102(b) based upon a public use or sale of the invention.

The specification at page 116 states that the nucleic acids of the present invention (including SEQ ID NO: 51) were procured from, and thereby known by Incyte Genomics Inc.

(via the Incyte Genomics LIFESEQ database) at the time the invention was made. Accordingly, the nucleic acids of the present invention were in public use and on sale in this country prior to the filing of the instant application. The nucleic acid appears to be cDNA from human samples (claims 2 and 4-5).

18. Claims 1-2 and 4-5 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter.

The specification at page 116 states that the nucleic acids of the present invention (including SEQ ID NO: 51) were procured from, and thereby known by Incyte Genomics Inc. (via the Incyte Genomics LIFESEQ database) at the time the invention was made. Accordingly, it appears that Applicant did not invent the claimed subject matter. The nucleic acid appears to be cDNA from human samples (claims 2 and 4-5).

19. Claims 1-2 and 4-5 are rejected under 35 U.S.C. 102(a) as being anticipated by Birren et al. (GenEmbl Accession No. AC032035).

Claims 1-2 and 4-5 are directed to nucleic acids comprising a nucleic acid sequence encoding SEQ ID NO: 174, "a" nucleic acid of SEQ ID NO: 51, nucleic acid molecules that "selectively hybridize" to a nucleic acid that encodes SEQ ID NO: 174 or "a" nucleic acid of SEQ ID NO: 51, and nucleic acids having at least 60% sequence identity to a nucleic acid sequence encoding SEQ ID NO: 174 or "a" nucleic acid of SEQ ID NO: 51.

Birren teaches GenEmbl Accession No. AC032035, which is 41.4% identical to Applicant's SEQ ID NO: 51, and has a best local similarity of 95.1% identity to Applicant's SEQ ID NO: 51 (see sequence search result #2). It is noted that the claims encompass nucleic acids comprising "a" nucleic acid of SEQ ID NO: 51, and therefore, GenEmbl Accession No.

AC032035 taught by Birren is considered to anticipate the claimed invention. In other words, because the claims recite "a" nucleic acid, the claims include portions (i.e., partial sequences) of SEQ ID NO: 51, wherein the portions may be of any length. Furthermore, because the claims recite, "comprising", the claims include nucleic acids, which contain this portion and an unlimited number of flanking nucleotides. Accordingly, because Birren teaches a nucleic acid that is 95.1% identical to a 185 base pair stretch of SEQ ID NO: 51 (including a stretch comprising at least one hundred and fifty identical base pairs, see sequence result #2), the teachings of Birren anticipate Claim 1. It is also noted that the nucleic acid of Birren would "selectively hybridize" to SEQ ID NO: 51, given the lack of clarity as to what conditions are considered to be conditions for "selective hybridization".

With respect to Claims 2 and 4-5, Birren teaches the nucleic acid is from a cDNA clone and that the nucleic acid is a mammalian (e.g., human) nucleic acid molecule (see sequence search result #2).

20. Claim 15 is rejected under 35 U.S.C. 102(b) as being anticipated by Mullis et al. (USPN 4,800,159).

Mullis et al. teach a kit comprising a means for determining the presence of the nucleic acid molecule of claim 1 in a sample of a patient (e.g., agent for polymerization, nucleoside triphosphates, means for detecting hybrids of a probe and a sequence, etc.) (see col. 3, for example).

Claim Rejections - 35 USC § 103

21. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

22. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (11746), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

23. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

24. Claims 7-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Incyte Genomics' LIFESEQ Database, as applied to claims 1-2 and 4-5 above, and further in view of Prendergast (USPN 5,958,753).

As discussed in the specification (pg. 116) the nucleic acids of the present invention (including SEQ ID NO: 51) were procured from, and thereby known by Incyte Genomics Inc. (via the Incyte Genomics LIFESEQ database) at the time the invention was made. The cited prior art does not teach expressing the nucleic acids using an expression system.

However, Prendergast teaches operably linking a polynucleotide into an expression vector, transforming a host cell with the resulting recombinant vectors and expressing the polypeptides encoded by the polynucleotide using the transformed host cells (see cols. 5-6, for example).

Accordingly, in view of the teachings of Prendergast, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have linked the polynucleotides of the LIFESEQ Database into expression vectors, to have transformed host cells with the resulting vectors and to have used the transformed cells to express polypeptides. One of ordinary skill in the art would have been motivated to do so in order to have provided an effective means for synthesizing polypeptides encoded by the isolated polynucleotides, which would have allowed for the further characterization of the functional properties of the isolated polynucleotides and the products encoded by the isolated polynucleotides.

25. Claims 7-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Birren et al. (GenEmbl Accession No. AC032035), as applied to claims 1-2 and 4-5 above, and further in view of Prendergast (USPN 5,958,753).

The teachings of Birren are presented above. Specifically, Birren teaches GenEmbl Accession No. AC032035 which has a best local similarity of 95.1% identity to Applicant's SEQ

ID NO: 51 (see sequence search result #2), and therefore, encompasses the claimed nucleic acid. Birren does not teach expressing the nucleic acids using an expression system.

However, Prendergast teaches operably linking a polynucleotide into an expression vector, transforming a host cell with the resulting recombinant vectors and expressing the polypeptides encoded by the polynucleotide using the transformed host cells (see cols. 5-6, for example).

Accordingly, in view of the teachings of Prendergast, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have linked the polynucleotides of Birren into expression vectors, to have transformed host cells with the resulting vectors and to have used the transformed cells to express polypeptides. One of ordinary skill in the art would have been motivated to do so in order to have provided an effective means for synthesizing polypeptides encoded by the isolated polynucleotides, which would have allowed for the further characterization of the functional properties of the isolated polynucleotides and the products encoded by the isolated polynucleotides.

Conclusion

26. No claims are allowable.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alexander H. Spiegler whose telephone number is (703) 305-0806 or (571) 272-0788 after January 22, 2004. The examiner can normally be reached on Monday through Friday, 7:00 AM to 3:30 PM.

If attempts to reach the examiner are unsuccessful, the primary examiner in charge of the prosecution of this case, Carla Myers, can be reached at (703) 308-2199 or at (571) 272-0747 after January 13, 2004. If attempts to reach Carla Myers are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119 or at (571) 272-0782 after January 22, 2004. The fax number for the organization where this application or proceeding is assigned is (703) 872-9306. Applicant is also invited to contact the TC 1600 Customer Service Hotline at (703) 308-0198.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Alexander H. Spiegler
December 24, 2003

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